Notice of Allowability	Application No.	Applicant(s)	
	10/753,136	HENEGAR, KEVIN EDWARD	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *telephonic interview 19 May 2005*.

2. ☒ The allowed claim(s) is/are *1, 3, 7 and 8*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

LEON B. LANKFORD, JR.
PRIMARY EXAMINER

RD

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Edward Robinson on 23 May 2005.

The application has been amended as follows:

Claim 1 has been re-written as:

-- Claim 1. A process for the preparation of enantiomerically enriched (1S,4R) 1-acetoxy-4-hydroxycyclopent-2-ene comprising the steps of:

a) determining the water content of pancreatin;

b) mixing pancreatin, *cis*-1,4-dihydroxycyclopent-2-ene, vinyl acetate, and triethylamine in tetrahydrofuran;

c) adjusting the water content of the mixture such that the water content is 5-7% of the weight of the pancreatin;

d) maintaining a reaction temperature of –40°C to +40°C with stirring until the reaction is substantially complete;

e) concentrating the reaction mixture

f) dissolving the residue in methyl-t-butylether, optionally treating the mixture with activated charcoal and filtering the mixture; and

g) precipitating (1S,4R) 1-acetoxy-4-hydroxycyclopent-2-ene with an enantiomeric purity of 95-99% by the addition of a hydrocarbon solvent at 0-15°C.--

Claim 3 has been re-written as:

-- Claim 3. A process for the preparation of enantiomerically enriched (1S,4R) 1-acetoxy-4-hydroxycyclopent-2-ene comprising the steps of:

a) determining the water content of pancreatin;

b) adjusting the water content of the mixture such that the water content is 5-7% of the weight of the pancreatin;

c) mixing pancreatin, *cis*-1,4-dihydroxycyclopent-2-ene, vinyl acetate, and triethylamine in tetrahydrofuran;

d) maintaining a reaction temperature of –40°C to +40°C with stirring until the reaction is substantially complete;

e) concentrating the reaction mixture

f) dissolving the residue in methyl-t-butylether, optionally treating the mixture with activated charcoal and filtering the mixture; and

g) precipitating (1S,4R) 1-acetoxy-4-hydroxycyclopent-2-ene with an enantiomeric purity of 95-99% by the addition of a hydrocarbon solvent at 0-15°C.--

Claim 7 has been re-written as:

-- Claim 7. A process according to claim 1 or claim 3 wherein the reaction temperature of step (d) is maintained between +5°C to +10°C. --

Please add new claim 8 as follows:

-- Claim 8. A process according to claim 1 or claim 3 wherein step (e) concentrating the reaction mixture is performed at 20-50°C bath temperature and 20-60 mm Hg pressure.--

Please cancel claims 2 and 4.

Please cancel the amendment to the specification submitted 17 March 2005, which replaced the paragraph at page 2, line 17 through page 3, line 14 as follows:

"The first step in the process is determining the water content of pancreatin. The water content may be determined by methods well known to those skilled in the art. These methods include the Karl-Fischer titration, and measurement of weight loss after careful drying. The Karl-Fisher titration is preferred because of its greater speed, and because it is not certain that only water is lost on drying. The pancreatin may, at this point, either be mixed with *cis*-1,4-dihydroxycyclopent-2-ene (Formula II),

Formula II

and triethylamine in a solvent, in which case the water content of the mixture is adjusted such that the water is 5-7 % by weight relative to pancreatin. Alternatively, the step of adjusting the water content of the pancreatin may take place before adding the pancreatin to the mixture. In this case, the water content of the pancreatin is adjusted such that the water is 5-7 % by weight relative to pancreatin, and then the pancreatin with its associated water is mixed with *cis*-1,4-dihydroxycyclopent-2-ene, vinyl acetate, and triethylamine in a solvent. Either order of addition of water leads to the same reaction mixture. The amount of pancreatin used in proportion to substrate is not fixed. The less pancreatin used, the slower the reaction. It has been found that approximately one gram of 8X pancreatin per gram of substrate provides a convenient ratio and allows the reaction to be substantially complete in 22–24 hours. Prancreatins of greater purity such as 10X may be used in proportionally lower amounts, while pancreatins of lower purity, such as 4X, may be used in proportionally larger amounts. ~~The man~~ **One** skilled in the art can readily determine what proportion of pancreatin relative to substrate to use, based upon the purity level of the pancreatin, and the speed of reaction desired. Vinyl acetate is used in molar excess compared to the starting material. A range of 5 to 7 moles of vinyl acetate per mole starting material is convenient. A level of 6 moles of vinyl acetate per mole starting material provides good results. The triethylamine is present in catalytic quantities. A range of 0.02 to 0.1 moles of triethylamine per mole starting material is convenient. A level of 0.05 moles of triethylamine per mole starting material provides good results."

Please replace paragraph at page 3, line 17 through page 4, line 14 as follows:

-- The first step in the process is determining the water content of pancreatin. The water content may be determined by methods well known to those skilled in the art. These methods include the Karl-Fischer titration, and measurement of weight loss after careful drying. The Karl-Fisher titration is preferred because of its greater speed, and because it is not certain that only water is lost on drying. The pancreatin may, at this point, either be mixed with *cis*-1,4-dihydroxycyclopent-2-ene (Formula II),

Formula II

and triethylamine in a solvent, in which case the water content of the mixture is adjusted such that the water is 5-7 % by weight relative to pancreatin. Alternatively, the step of adjusting the water content of the pancreatin may take place before adding the pancreatin to the mixture. In this case, the water content of the pancreatin is adjusted such that the water is 5-7 % by weight relative to pancreatin, and then the pancreatin with its associated water is mixed with *cis*-1,4-dihydroxycyclopent-2-ene, vinyl acetate, and triethylamine in a solvent. Either order of addition of water leads to the same reaction mixture. The amount of pancreatin used in proportion to substrate is not fixed. The less pancreatin used, the slower the reaction. It has been found that approximately one gram of 8X pancreatin per gram of substrate provides a convenient ratio and allows the reaction to be substantially complete in 22–24 hours. Prancreatins of greater purity such as 10X may be used in proportionally lower amounts, while pancreatins of lower purity, such as 4X, may be used in proportionally larger amounts. ~~The man~~ **One** skilled in the art can readily determine what proportion of pancreatin relative to substrate to use, based upon the purity level of the pancreatin, and the speed of reaction desired. Vinyl acetate is used in molar excess compared to the starting material. A range of 5 to 7 moles of vinyl acetate per mole starting material is convenient. A level of 6 moles of vinyl acetate per mole starting material provides good results. The triethylamine is present in catalytic quantities. A range of 0.02 to 0.1 moles of triethylamine per mole starting material is convenient. A level of 0.05 moles of triethylamine per mole starting material provides good results. --

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford
Examiner
Art Unit 1651